

## Synthesis and Spectroscopic Properties of 1-(Arylthioalkyl)benzotriazoles and Vinyl Sulphides

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**Summary:** A number of 1-(arylthioalkyl)benzotriazoles (2) and (6) have been prepared from compounds (1) and (5) respectively during reaction with BuLi and alkyl halides. The 1-(arylthioalkyl)benzotriazoles (2) and (6) were smoothly converted into their respective vinyl sulphides (3), (4) and (7) upon reaction with BF<sub>3</sub>-OEt<sub>2</sub>.

### Introduction

Although the importance of alkyl and arylthio ethers as biological building blocks is supreme and many of the possible derivatives have been extensively investigated, there is surprisingly little work on the chemistry of 1-(arylthioalkyl)benzotriazoles [1]. Recently pyrazole has been developed as a highly efficient synthetic auxiliary group for various chemical transformations [2]. The ability of the N-alkyl group in heterocyclic compounds to undergo lithiation is powerfully increased by suitable activating groups as in 1-(arylthiomethyl)pyrazole [2] and 9-(phenylthiomethyl)carbazoles [3]. We have recently reported the preparation of a number of novel vinyl sulphides [4] using the general lithiation procedure [1,2]. In continuation to our studies on the synthetic applications of 1-(arylthioalkyl) benzotriazoles (2) and (6) [4] the present work describes the preparation of further examples of these systems and their identification by <sup>1</sup>H, <sup>13</sup>C-NMR, mass spectra and elemental analysis.

### Results and Discussion

#### Alkylation of 1-(Arylthioalkyl)benzotriazoles

1-(Arylthioalkyl)benzotriazoles (1) and (5) react with BuLi at -78°C, the carbanion can be

trapped by various electrophiles (Scheme 1 and 2); ethyl iodide, n-butyl chloride and allyl bromide forming the alkylated products (2a-b) and (6a) respectively in good yield (Table 1). With benzophenone as an electrophile, the vinyl thioether (7b) was isolated along with a small amount of other products. This may well be due to the formation of compound (6b) as an intermediate, and the subsequent elimination of the benzotriazole entity in resulting vinyl thioether (7b). Compound (7b) was fully characterized by its <sup>1</sup>H, <sup>13</sup>C-NMR and elemental analysis. The <sup>1</sup>H-NMR spectrum shows two broad singlets (5.93 and 5.74 ppm) for OH protons, which disappear by addition of D<sub>2</sub>O, and three singlets (2.26, 2.07 and 2.06 ppm) for the two methyl groups indicate that the vinyl thioether (7b) is a 1:1 mixture of cis-trans isomers.

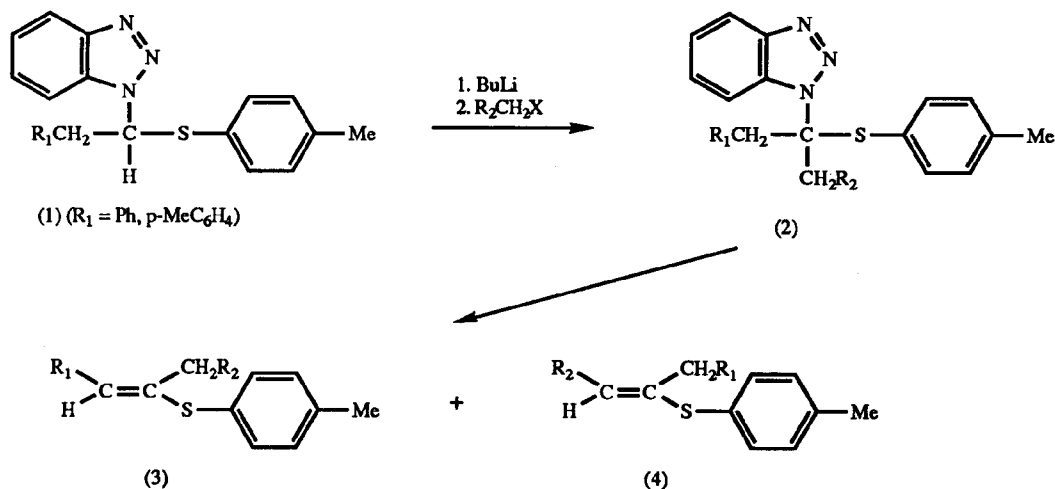
Compounds (2a-b) and (6a) were characterized by <sup>1</sup>H, <sup>13</sup>C-NMR, high resolution mass spectra or elemental analysis. The chemical shifts and multiplicities of the <sup>1</sup>H-NMR signals of R<sub>1</sub>CH<sub>2</sub> and R<sub>2</sub>CH<sub>2</sub>, attached to an asymmetric carbon, are also indicative of the product structure.

In the <sup>1</sup>H-NMR of compounds (2a-b) and (6a) the methyl protons resonate as a singlet in the

Table 1: Synthesis of 1-(Arylthioalkyl)benzotriazoles (2) and (6) and vinyl sulphides (3), (4) and (7).

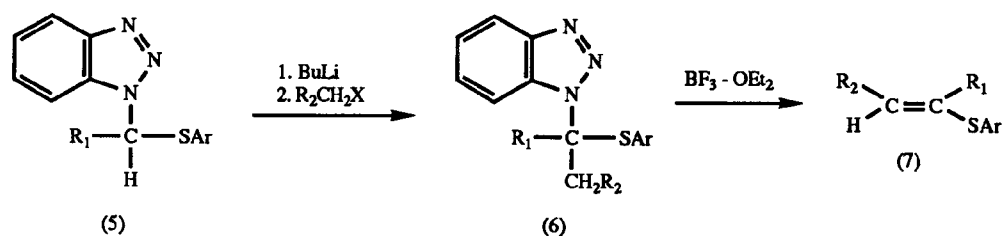
Compd.	Yield (%)	Sol. for recryst.	M.P. °C	Formula	Require					
					Found C	H	N	C	H	N
(2a)	70	MeOH	50-52	C <sub>23</sub> H <sub>23</sub> N <sub>3</sub> S	73.90	6.16	11.26	74.04	6.39	11.38
(2b)	81	Converted into (3b) and (4b) without purification.								
(3a, 4a)	62	By column oil		C <sub>17</sub> H <sub>18</sub> S	254.1129			H.R.M. 254.1127		
(3b, 4b)	71	By column oil		C <sub>20</sub> H <sub>24</sub> S	81.03	8.16	--	80.93	8.21	--
(6a)	65	E.P.E	130-132	C <sub>22</sub> H <sub>19</sub> N <sub>3</sub> S	73.95	5.32	11.76	74.15	5.38	11.68
(7a)	61	By column oil		C <sub>16</sub> H <sub>14</sub> S	239.089			H.R.M. 239.085		
(7b)	50	MeOH	108-110	C <sub>29</sub> H <sub>26</sub> S	82.46	6.16	--	82.17	6.43	--

(E.P.E. is a mixture of ether petroleum ether (50%), H.R.M. means high resolution mass spectra)



Compounds 2-4, (a)  $R_1 = \text{Ph, } R_2 = \text{Me}$  (b)  $R_1 = \text{p-MeC}_6\text{H}_4, R_2 = \text{C}_3\text{H}_7$

Scheme-1



Compounds 5-7 are (a)  $\text{Ar} = R_1 = \text{Ph, } R_2 = \text{CH}=\text{CH}_2$  (b)  $\text{Ar} = R_2 = \text{p-MeC}_6\text{H}_4, R_1 = \text{Ph}_2\text{COH}$

Scheme-2

range 1.92-2.23 ppm (Table 2). Typically, the benzotriazole protons [5-7] and aromatic protons absorbed in the range 7.23 - 8.33 ppm as complex multiplets. The  $\text{ArCH}_2$  protons were diastereotopic due to the linkage of methylene group to an asymmetric tertiary carbon, thus providing a doublet of doublets due to the geminal AB type of coupling. Similarly compounds (2a-b) also displayed additional two sets of multiplets for methylene protons linked to an asymmetric carbon and methyl or propyl group.

In the  $^{13}\text{C-NMR}$  six signals for the benzotriazole [7-9] and eight signals for aromatic carbons were assigned by comparison with similar

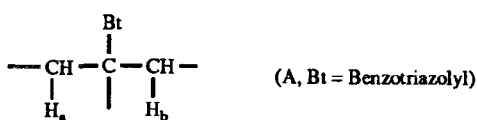
systems (Table 3). Generally, the most indicative tertiary carbon signal was observed in a range from 78.5 to 79.4 ppm.

#### *Transformation of 1-(Arythioalkyl)benzotriazoles into vinyl sulphides*

In order to utilize the arythio and benzotriazolyl moieties for activation of the N-C- $\text{CH}_2$ -group, the selective removal of benzotriazolyl group from the tertiary carbon under mild conditions was investigated. Compounds (2a-b), having two active methylene groups, react with  $\text{BF}_3\text{-OEt}_2$  solution at room temperature giving a mixture of vinyl sulphides (3) and (4) (Scheme 1). B- $\text{H}_a$  as well as B-

Table 2:  $^1\text{H}$ -NMR chemical shifts of the 1-(Arylthioalkyl) benzotriazoles (2) and (6) and vinyl sulphides (3), (4) and (7) in  $\text{CDCl}_3$  with reference  $\text{Me}_4\text{Si}$ .

Compd.	Aromatic-H	$\text{R}_1\text{CH}/\text{R}_2\text{CH}$	$\text{R}_1\text{CH}_2/\text{R}_2\text{CH}_2$	Other-H
(2a)	8.13 (d, J=8.4, 1H), 7.40 (d, J=8.4, 1H), 7.31 (t, J=7.1, 1H), 7.20 (t, J=7.1, 1H), 6.99 (m, 3H), 6.81 (d, J=8.4, 2H), 6.45 (m, 4H).	-	3.77 (d, J=14.5), 3.28 (d, J=14.5), 2.30(m); 1.95 (m)	1.92 (s, 3H), 1.24 (t, J=5.3, 3H)
(2b)	8.31 (d, J=8.4, 1H), 8.04 (d, J=8.4, 1H), 7.45 (m, 2H), 6.91 (m, 4H), 6.63 (m, 4H).	-	3.98 (d, J=14.4), 3.50 (d, J=14.4), 2.50 (m), 1.95 (m)	2.23 (s, 3H), 2.12 (s, 3H), 2.02 (m, 1H), 1.52 (m, 1H), 1.30 (m, 2H), 0.91 (m, 3H),
(3a)	7.51 (d, J=7.6, 1H), 7.31-7.0 (m, 17H).	6.72(s), 6.53(s)	2.92 (q, J=7.4),	2.20 (s, 6H), 1.24 (t, J=5.4, 6H)
(3b)	7.41 (d, J=8.0, 1H), 7.33 (d, J=8.0, 1H), 7.25-7.0 (m, 12H), 6.95 (d, J=8.0, 2H).	6.68(s), 6.52 (s)	2.31(m), (m)	2.14 2.23 (s, 6H), 2.20 (s, 6H), 1.25 (m, 8H), 0.90 (m, 6H)
(4a)	7.55 (d, J=7.6, 1H), 7.31-7.0 (m, 17H)	5.96(m), 5.85(m)	3.41(s), 3.83 (s)	2.21 (s, 6H), 1.81 (d, J=6.6, 3H), (d, J=6.6, 3H)
(4b)	7.45 (d, J=8.0, 1H), 7.35 (d, J=8.0, 1H), 7.25-7.0 (m, 12H), 6.96 (d, J=8.0, 2H).	5.82 (t, J=7.1), 5.77 (t, J=7.1)	3.52(s), 3.45(s) (s)	2.26 (s, 6H), 2.21 (m, 4H), 2.07 (s, 3H), 2.05 (s, 3H), 1.41 (m, 4H), 0.85 (m, 6H)
(6a)	8.06 (d, J=8.1, 1H), 8.02 (d, J=8.1, 1H), 7.66 (d, J=8.1, 1H), 7.52=7.0 (m, 9H), 6.70 (d, J=8.1, 2H).		5.02 (d, J=5.3), 4.90 (d, J=5.3)	5.87 (m, 1H), 3.54 (m, 2H)
(7a)	7.66-6.90 (m, 20 cis-trans-H).	6.39(m)		6.30 (m, 2H), 5.50 (d, J=16.8, 1H), 5.32 (d, J=10.1, 1H), 5.18 (d, J=16.8, 1H), 5.0 (d, J=10.1, 1H)
(7b)	7.75 (m, 8H), 7.40 (m, 10H), 7.13 (d, J=7.9, 2H), 7.04 (d, J=7.9, 2H), 7.0-6.51 (m, 14H).	6.45(s), 6.37 (s)		5.93 (br.s, OH), 5.74 (br.s, OH), 2.26 (s, 6H), 2.07 (s, 3H), 2.06 (s, 3H)



$\text{H}_b$ , in the general structure A, are eliminated with Bt (benzotriazolyl) leaving group giving isomeric vinyl sulphides (3) and (4). The isomeric compounds (3) and (4) were fully characterized by  $^1\text{H}$  and  $^{13}\text{C}$ -NMR study. All attempts for their separation were unsuccessful because the mixture indicated a single spot on the t.l.c. plate. Compound (6a), with only one methylene group, react with  $\text{BF}_3 \cdot \text{OEt}_2$  giving vinyl sulphide (7a) (Scheme 2) in 61% yield (Table 1). Vinyl sulphide (7a) was fully characterized by  $^1\text{H}$ ,  $^{13}\text{C}$ -NMR and elemental analysis.

### $^1\text{H}$ and $^{13}\text{C}$ -NMR of vinyl sulphides (3), (4) and (7)

Spectral analysis of the vinyl sulphides in this work allowed easy structure elucidation. In most instances, correct structure determination were obtained by  $^1\text{H}$ -NMR spectrum (Table 2). Any ambiguities in the assigned structures were clarified by the  $^{13}\text{C}$ -NMR spectrum (Table 4).

In the  $^1\text{H}$ -NMR spectrum of the vinyl sulphides (3a-b) and (7b) the ArCH proton resonated as a pair of singlets in the range of 6.37- 6.72 ppm (Table 2) while compounds (4a-b) displayed two sets of triplets and multiplets. The vinyl sulphides (3), (4) and (7) were found to be approximately 1:1 mixture of cis-trans isomers. Interestingly, the symmetrical vinyl sulphide (7a) indicated only a multiplet at 6.39 ppm.

Table 3:  $^{13}\text{C}$ -NMR chemical shifts of the 1-(arythioalkyl) benzotriazoles (2) and (6)<sup>a</sup>

Compd.	Benzotriazole-C						Aromatic-C	Other-C
	C-3a	C-4	C-5	C-6	C-7	C-7a		
(2a)	146.5	120.2	124.0	127.2	114.3	132.6	139.6, 134.9, 134.3, 129.6, 129.5, 129.1, 126.8, 126.7	79.4, 40.3, 26.9 21.0, 8.6
(2b)	146.8	120.3	123.9	126.8	114.4	132.6	139.6, 136.8, 135.0, 129.6, 129.5, 129.4, 129.0, 128.7	78.9, 40.5, 35.1, 26.1, 25.3, 22.7, 21.1, 14.1
(6a)	146.7	119.6	124.0	127.2	114.2	131.8	133.3, 129.1, 126.9, 128.8, 128.5, 126.9, 126.6, 120.1	136.5, 111.8, 78.5,

<sup>a</sup> In  $\text{CDCl}_3$  with reference  $\text{Me}_4\text{Si}$ .Table 4:  $^{13}\text{C}$ -NMR chemical shifts of the vinyl sulphides (3), (4) and (7)<sup>1</sup>

Compd.	Vinyl, Dienyl and Aromatic-C	Other-C
(3a,4)	139.2, 137.4, 137.2, 136.9, 136.4, 136.1, 135.8, 134.3, 133.9, 132.8, 132, 131.7, 131.6, 131.2, 131.0, 130.4, 130.3, 130.0, 129.9, 129.8, 129.7, 129.7, 129.6, 129.5, 129.4, 129.3, 129.2, 129.1, 129.0, 128.9, 128.5, 128.3, 128.2, 128.1, 127.9, 126.9, 126.8, 126.5, 126.2, 126.1	43.5, 31.2, 28.3, 24.7, 12.1, 21.0, 20.9, 20.8, 15.6, 14.5, 13.9, 13.8
(3b,4b)	139.5, 137.3, 136.7, 136.6, 136.5, 136.4, 136.2, 136.1, 136.0, 135.9, 135.6, 135.5, 135.4, 134.4, 133.9, 133.7, 133.4, 132.5, 131.4, 131.3, 131.0, 130.6, 130.4, 129.8, 129.7, 129.6, 129.5, 129.4, 129.1, 128.9, 128.8, 128.7, 128.6, 128.4, 128.3, 128.2, 127.8, 126.7, 126.4, 126.2	42.9, 37.3, 36.1, 31.8, 31.4, 31.2, 31.0, 30.9, 22.8, 22.6, 22.4, 21.9, 21.2, 21.1, 21.0, 20.9, 13.9, 13.8
(7a)	138.6, 137.0, 134.6, 133.5, 132.1, 130.7, 129.8, 129.6, 129.0, 128.9, 128.8, 128.7, 128.6, 128.4, 128.3, 128.1, 128.0, 128.0, 127.6, 127.5, 127.3, 127.1, 125.5, 118.0	--
(7b)	169.8, 169.6, 147.2, 145.4, 142.5, 142.3, 137.9, 137.7, 137.3, 133.4, 133.0, 132.1, 130.3, 129.9, 129.5, 129.1, 129.0, 128.9, 128.7, 128.1, 128.0, 127.9, 126.3, 125.3, 124.4, 123.6, 119.5, 118.9	84.1, 83.7, 21.0, 20.9, 20.8

<sup>a</sup> In  $\text{CDCl}_3$  with  $\text{Me}_4\text{Si}$  as the reference.

In the  $^{13}\text{C}$ -NMR of the vinyl sulphides (3), (4) and (7) the aliphatic carbons appear in the range from 13.8 to 43.5 ppm (Table 4). The  $\text{Sp}^2$  regions, both the allylic and aromatic, were rather complex due to the presence of cis-trans isomers. The aromatic and allylic carbons assignments are uncertain because of the small chemical shifts difference between the signals.

### Experimental

The melting points were measured either with a hot-stage microscope or a capillary melting point apparatus and are uncorrected.  $^1\text{H}$  and  $^{13}\text{C}$ -NMR spectra were recorded on a Varian EM 360L (200 MHz) spectrometer using  $\text{Me}_4\text{Si}$  as an internal standard. High resolution mass spectra were determined on a AEJ MS30 mass spectrometer. Tetrahydrofuran (THF) was distilled from sodium-benzophenone prior to use.

The following compounds were prepared by the literature general method quoted. 1-(Arythioalkyl)benzotriazoles (1) and (5) [4].

### General procedure for lithiation of 1-(arythioalkyl)benzotriazoles (1) and (5) and subsequent trapping by electrophiles

To 1-(arythioalkyl)benzotriazoles (1) and (5) (0.01 mol) in dry THF (50 ml) was added BuLi (1.5 M in hexane, 8.0 ml, 0.012 mol) at  $-78^\circ\text{C}$  under argon and the solution stirred for 1.5h. The required electrophile (0.01 mol) in dry THF (20 ml) was added at  $-78^\circ\text{C}$  and the reaction mixture stirred at  $-78^\circ\text{C}$  (4.0 h) and at room temperature (12 h). Aqueous solution of  $\text{NH}_4\text{Cl}$  (20%, 100 ml) was added and extracted with  $\text{CH}_2\text{Cl}_2$  (2x50 ml). Evaporation of organic layer, after drying over  $\text{MgSO}_4$ , gave oily residue or solid products. The oily residue solidified on trituration with petroleum ether, which on recrystallization from the appropriate solvent or by column chromatography gave (2) and (6) respectively (Table 1).

### Preparation of vinyl sulphides (3), (4) and (7)

To 1-(arythioalkyl) benzotriazoles (2) and (6) (0.01 mol.) in dry diethyl ether (50 ml) was added

BF<sub>3</sub>-OEt<sub>2</sub> solution (1.0 ml) and stirred for 6-8h at room temperature. The mixture was poured into aqueous Na<sub>2</sub>CO<sub>3</sub> solution (20%, 100 ml) and extracted with diethyl ether (2x50 ml). Rotoevaporation of the organic solvent, after drying over MgSO<sub>4</sub>, gave vinyl sulphides along with undesired products. Column chromatography of the crude products on silica gel using hexane-chloroform (1:1) as eluent gave vinyl sulphides (3), (4) and (7) in 50-70% yield (Table 1).

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